

53. (Currently AmendedNew)

An oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising at least two CpG moieties and a nucleoside antimetabolite covalently linked to the oligonucleotide

The oligonucleotide of claim 51, wherein the antimetabolite is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, pentostatin and a nucleoside antimetabolite for 2'-deoxy, 2',2'-difluorocytidine.

54. (Currently AmendedNew)

The oligonucleotide of claim 51 or 53, wherein two of said

at least two CpG

moieties are separated by a number of nucleotides selected from the numbers 2, 5, and 9.

55. (Currently AmendedNew)

The oligonucleotide of claim 51 or 53, wherein said

nucleoside antimetabolite is 5' to said at least two CpG moieties.

56. (Currently AmendedNew)

The oligonucleotide of claim 51 or 53, wherein said

nucleoside antimetabolite is 3' to said at least two CpG moieties.

57. (Currently AmendedNew)

The oligonucleotide of claim 51 or 53, wherein said

nucleoside antimetabolite is 3' to at least one CpG moiety and 5' to at least a second CpG

moiety.

58. (Currently AmendedNew)

The oligonucleotide of claim 51 or 53, wherein said

nucleoside antimetabolite is linked to the oligonucleotide by a 3'-3' linkage.

59. (Currently AmendedNew)

The oligonucleotide of claim 51 or 53, wherein said

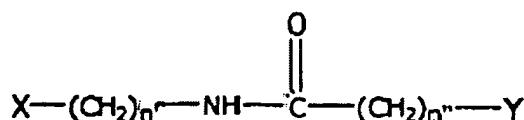
nucleoside antimetabolite is linked to the oligonucleotide by a 5'-5' linkage.

60. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 3'-5' linkage.

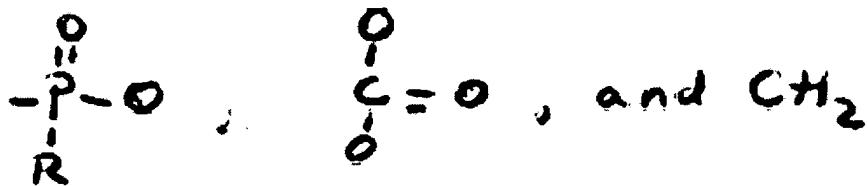
61. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is covalently linked to the oligonucleotide by a 5'-3' linkage.

62. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is at a position that is selected from the following positions: 10 nucleotides upstream from one of the at least two CpG moieties, 9 nucleotides upstream from the CpG moiety, 8 nucleotides upstream from the CpG moiety, 7 nucleotides upstream from the CpG moiety, 6 nucleotides upstream from the CpG moiety, 5 nucleotides upstream from the CpG moiety, 4 nucleotides upstream from the CpG moiety, 3 nucleotides upstream from the CpG moiety, 2 nucleotides upstream from the CpG moiety, 1 nucleotides upstream from the CpG moiety, 10 nucleotides downstream from a CpG moiety, 9 nucleotides downstream from the CpG moiety, 8 nucleotides downstream from the CpG moiety, 7 nucleotides downstream from the CpG moiety, 6 nucleotides downstream from the CpG moiety, 5 nucleotides downstream from the CpG moiety, 4 nucleotides downstream from the CpG moiety, 3 nucleotides downstream from the CpG moiety, 2 nucleotides downstream from the CpG moiety, and 1 nucleotides downstream from the CpG moiety.

63. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein the nucleoside antimetabolite is covalently linked to the oligonucleotide by a linker having the formula.



wherein x and y are independently selected from



and R is selected from H, S, a C₁-C₆ alkyl, a C₁-C₆ alkoxy, and NH.

64. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one nucleotide having a ribose sugar moiety.

65. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one nucleotide having a 2'-deoxyribose sugar moiety.

66. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one 2'-halogen nucleotide.

67. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one 2'-N-alkyl nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms.

68. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one 2'-O-alkyl nucleotide, one 2'-N-Alkyl nucleotide, or one 2'-O-halogen nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms

69. (NewPreviously presented) The oligonucleotide of claim 68, wherein the alkyl is methyl.

70. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises a plurality of nucleotides connected by covalent internucleoside linkages, wherein each of the linkages are selected from the group consisting of a phosphodiester

linkage, a C1-C6 alkoxy phosphotriester linkage, a phosphorothioate linkage and a phosphoramidate linkage.

71. (Currently AmendedNew) A pharmaceutical composition comprising the oligonucleotide of any of claims 51 or 53-70.

72. (Previously presentedNew) A pharmaceutical composition of claim 71 further comprising a pharmaceutically acceptable carrier.

73. (Previously presentedNew) The oligonucleotide of claim 72 wherein said pharmaceutically acceptable carrier is lipofectin.

74. (Previously presentedNew) An oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising a motif represented by one of the group of formulas 5'-PCGXCG-3' and 5'-CGXCGP-3', and wherein P is a nucleoside antimetabolite and X represents between 0 and 50 nucleotides.

775. (Currently AmendedNew)

An oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising a motif represented by one of the group of formulas 5'-PCGXCG-3' and 5'-CGXCGP-3', and wherein X represents between 0 and 50 nucleotides and P is a nucleoside
The oligonucleotide of claim 74, wherein the antimetabolite is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, pentostatin and 2'-deoxy, 2',2' -difluorocytidine.

76. (Currently AmendedNew) The oligonucleotide of claim of 74 or 75, where X is selected from the group consisting of 2, 5, and 9 nucleotides.

77. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 3'-3' linkage.

78. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 5'-5' linkage.

79. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 3'-5' linkage.

80. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises 10 multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 5'-3' linkage.

81. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises at least one nucleotide having a ribose sugar moiety.

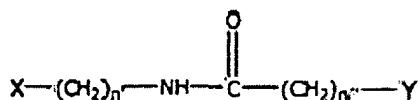
82. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises at least one nucleotide having a 2'-deoxyribose sugar moiety.

83. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises at

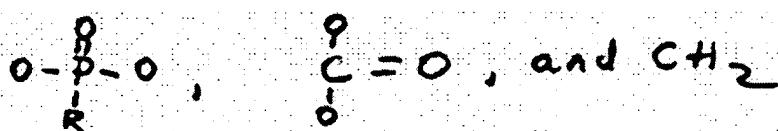
least one 2'-0-Alkyl nucleotide, 2'-N-Alkyl nucleotide, or 2'-0-halogen nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms.

84. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises a plurality of nucleotides connected by covalent internucleoside linkages, wherein the linkages are selected from the group consisting of phosphodiester linkage, a C1-C6 alkoxy phosphotriester linkage, a phosphorothioate linkage and a phosphoramidate linkage.

85. (Currently AmendedNew) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises 30 multiple nucleotides and the nucleoside antimetabolite is attached to at least one of the multiple nucleotides by a linker having the formula.



wherein x and y are independently selected from



and R is selected from H, S, a C1-C6 alkyl, a C1-C6 alkoxy, and NH.

86. (Currently AmendedNew) A pharmaceutical composition comprising the oligonucleotide of any of claims 74-85.

87. (Currently AmendedNew) A pharmaceutical composition of claim 86-74 further comprising a pharmaceutically acceptable carrier.

88. (Currently AmendedNew) The oligonucleotide of claim 876 wherein said pharmaceutically acceptable carrier is lipofectin.

89. (Previously presentedNew) The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over non- cancerous cells comprising the steps of:

- (a) Selecting a oligonucleotide comprising at least two CpG moieties; and
- (b) Covalently linking a nucleoside antimetabolite to said oligonucleotide comprising at least two CpG moieties.

90. (CanceledNew) ~~The method of claim 89, wherein said oligonucleotide comprising at least two CpG moieties comprises between 2 and 50 nucleotides.~~

91. (Currently AmendedNew)

The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over non- cancerous cells comprising the steps of:

- (a) Selecting a oligonucleotide comprising at least two CpG moieties; and
- (b) Covalently linking a nucleoside antimetabolite to said oligonucleotide comprising at least two CpG moieties,

The method of claim 89, wherein said nucleoside antimetabolite is - selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, pentostatin and antimetabolite for 2'-deoxy, 2',2'-difluorocytidine.

92. (New) The method of claim 89 or 91, wherein said oligonucleotide comprising at least two CpG moieties comprises between 2 and 50 nucleotides.